

II. REMARKS

Upon entry of the amendment, claims 1 to 10 and 50 to 64 will be pending. A marked-up copy showing the amendments to claims 1 and 5 is attached hereto as Exhibit A.

A. Regarding the Amendments

Claim 1 has been amended to clarify that a "specific cell type" obtained by a method of the invention is a "specific progenitor cell type". The amendment is supported, for example, at page 32, line 19, to page 33, line 19. As such, the amendment does not add new matter.

Claim 5 has been amended to clarify that reference to an antibody "derivative" refers to an "antigen binding fragment" of an antibody. The amendment is supported, for example at page 12, line 14, to page 13, line 7, and page 14, lines 5-8 of the specification. As such, the amendment does not add new matter.

New claims 58 to 64 have been added. New claims 58, 59 and 61 to 63 are supported, for example, at page 32, lines 19-23. New claims 60 and 64 are supported, for example, at page 36, lines 11-20, and by Table 1 (page 48). As such, the newly added claims do not add new matter.

B. Rejections under 35 U.S.C. § 112

The rejections of the claims under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite are respectfully traversed.

It is stated in the Office Action that the term "substantially enriched" is a relative term which renders the claim indefinite. Applicant maintains, for reasons of record, that any amount of enrichment from the state in which the specific cell type naturally occurs is sufficient to meet the limitation, and that one skilled in the art reading the claims in view of the specification would

know that a method of the invention, which separates a specific cell type based on its binding to an agent that binds specifically to cells expressing a serpentine receptor, results in a composition that is substantially enriched in the specific cell type.

It is submitted that the term "substantially" does not necessarily make a claim indefinite under 35 U.S.C. § 112, second paragraph. In this respect, the Federal Circuit held that a patent was not invalid for indefiniteness even though the applicant used the words "substantially equal" in the claim. Andrew Corp. v. Gabriel Electronics, Inc., 847 F.2d 819 (Fed. Cir. 1988). In Andrew Corp., the Court reasoned that "[t]he criticized words are ubiquitous in patent claims. Such usages, when serving reasonably to describe the claimed subject matter to those of skill in the field of the invention, and to distinguish the claimed subject matter from the prior art, have been accepted in patent examination and upheld by the courts." Id. at 821. More recently, it was held that use of the word "substantially" does not necessarily render the claim indefinite. Bausch & Lomb, Inc. v. Alcon Laboratories, Inc., 79 F.Supp.2d 243 (W.D. N.Y. 1999). There, the court found that the claim at issue was valid because "a person of ordinary skill in the art would understand what is claimed in the patent, notwithstanding the absence of any specific definition or numerical quantification of the phrase, 'does not substantially inhibit.'" Id. at 247-247. Therefore, use of the term "substantially" in a claim, even without a specific definition or numerical quantification, does not necessarily make a claim indefinite 35 U.S.C. § 112, second paragraph.

In summary, it is maintained that the use of the term "substantially" in the claims does not render the claimed subject matter vague and indefinite because the skilled artisan, reading the claims, would know that "a composition substantially enriched in a specific cell type" is one that is obtained using a binding agent specific for a serpentine receptor to separate such cells from a sample, and because the courts have recognized that the term "substantially" does not necessarily

render a claim vague. Accordingly, it is respectfully requested that the Examiner reconsider and remove this ground of rejection.

It is also stated in the Office Action that the term "binding agent" is not defined and, therefore, the metes and bounds of "binding agent" cannot be determined. Applicant maintains, for reasons of record, that the metes and bounds of "binding agent" can be determined because the claims require that a "binding agent binds specifically" to a cell or cells expressing a serpentine cell surface receptor, and because the specification provides examples of such binding agents, including, for example, a ligand or an antibody specific for a cell surface marker (see page 3, lines 1-5). Further in this respect, it is submitted that the skilled artisan, having selected a serpentine receptor to use as a means to obtain a cell type, would know ligands or other specific binding agents that specifically bind to the receptor. Accordingly, it is submitted that the claimed subject matter would be clearly understood by the skilled artisan and, therefore respectfully requested that this ground of rejection be removed.

It is also stated in the Office Action that the term "or derivative thereof" in claim 5 is unclear. Applicant maintains, for reasons of record, that the term "derivative" is not unclear or indefinite when the claim is read in view of the specification. Nevertheless, in order to advance prosecution of the subject application, claim 5 has been amended to clarify that the claimed subject matter includes an "antigen binding fragment" of an antibody. As such, it is respectfully requested that this rejection be removed.

In view of the amendment to claim 5 and the above remarks, and further in view of the specification and of knowledge in the art, it is submitted that the claims clearly define the subject matter regarded as the invention such that one skilled in the art would know the metes and

bounds of the claimed subject matter. Accordingly, it is respectfully requested that the rejections of the claims under 35 U.S.C. § 112, second paragraph, be removed.

C. Prior Art Rejections

The rejection of claims 1 to 10, and 50 to 57 under 35 U.S.C. § 103(a) as allegedly obvious over Nef and Nef, or Drutel et al., or Vanderhaeghen et al, or Mombaerts et al, in view of Janeway and Travers, or Stites et al., or Schlossman et al., or Seed et al., or Wysocki et al., or Aruffo et al., or Heller et al., or Foote, U.S. Patent No. 5,661,028 is respectfully traversed.

The present invention is based on Applicant's discovery that serpentine receptors, e.g., olfactory receptors, are expressed on essentially all cell types, thus indicating that the serpentine receptors have a role beyond, e.g., olfaction. As disclosed in the subject application, serpentine receptors have a widespread and central role in embryogenesis, wherein they act, via homophilic and heterophilic interactions, to direct organogenesis (see, for example, page 40, line 23, to page 41, line 15; and page 45, lines 10-13). As such, the present invention provides the qualitatively new discovery that serpentine receptors are involved in defining a specific lineage for which a cell is determined. By analogy to a telephone number, which includes, for example, an area code, a three digit prefix, and a four digit extension, serpentine receptors are disclosed as providing cell lineage specificity, similar to the specificity conferred by the four digits extension of a telephone number. As such, the present invention provides methods of a specific progenitor cell type using a binding agent specific for a serpentine receptor indicative of the progenitor cell type, which is programmed to develop along a particular lineage.

Amended claims 1 to 10, and new claims 58 to 60, are directed to a method of obtaining a composition substantially enriched for a specific progenitor cell type, in part, by using at least one binding agent specific for a serpentine cell surface receptor. Claims 50 to 57, and new claims 61 to 64, are directed to a method as in claim 1, further including separating from the cells

obtained using the at least one binding agent, those cells that express at least one additional marker (see, also, claim 2), and, in one embodiment, wherein the cells are a specific progenitor cell type.

It is maintained in the Office Action that, based on the Nef and Nef, Drutel et al., Vanderhaegen et al., and Mombaerts et al. references, which describe that certain cell types express certain receptors; and on the Janeway and Travers, Stites et al., Seed et al., Schlossman et al., Wysocki et al, and Foote reference, which variously describe methods to identify and separate a cell type bound to a marker, it would have been prima facie obvious to one of skill in the art to sort and analyze the olfactory (serpentine) marker expressing cells to obtain an enriched composition because one of skill in the art would be motivated to do so by such prior art references. It is further stated that there are a multitude of motivations for sorting cells to obtain an enriched cell population, including, for example, to study expression of a receptor by the cell, and to obtain a specific cell type useful in treating a disease.

With respect to previously pending claims 1 and 4 to 10, Applicant maintains, for reasons of record, that one of ordinary skill in the art would not have been motivated to combine the cited references because there is nothing in the references themselves, or in the art in general, that would have led the artisan to combine the references. The Federal Circuit has held that "when a rejection depends on a combination of prior art references, there must be some teaching, suggestion or motivation to combine the references." In re Rouffet, 149 F.3d 1350, 1355 (Fed. Cir. 1998). In Rouffet, the Court reviewed a decision by the Board of Patent Appeals and Interferences finding a claim obvious in light of the prior art. Id. at 1354. The Board maintained, and the Court agreed, that the prior art, in the aggregate, contained all of the elements contained in the rejected claim. Id. at 1357. Nevertheless, the Court determined that "the Board reversibly erred in determining that one of skill in the art would have been motivated to combine [the prior

art] references in a manner that rendered the claimed invention obvious." Id. The Court noted that virtually all inventions are combinations of old elements and that, therefore, an examiner may often find every element of a claimed invention in the prior art. As such, the Court reasoned that if the patent office rejected patents solely because each claimed element was in the prior art, the examiner could "use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention." Id. Thus, in order to prevent such "hindsight analysis", the Court held that the examiner must show a motivation to combine the references that create the case of obviousness. Id.

More recently, the Federal Circuit expanded on the In re Rouffet standard by holding that there must be a showing of actual evidence of motivation to combine the references - "That is, the showing must be clear and particular. [citations omitted.] Broad conclusory statements regarding the teaching of multiple references, standing alone, are not 'evidence.'" In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999). In Dembiczak, the Court noted that the Board's decision to reject a claim was "limited to a discussion of the ways that the multiple prior art references can be combined to read on the claimed invention . . . [y]et this reference-by-reference, limitation-by-limitation analysis fails to demonstrate how the [prior art] references teach or suggest the combination" Id. at 1000.

Applicant respectfully maintains that, in the present case, broad conclusory are made with respect to a motivation to combine the cited reference. Thus, it is alleged, for example, that one in the art would have been motivated to obtain a composition substantially enriched in a specific cell type, as claimed, because such cells could be used in the treatment of a disease. However, there is no indication in the Office Action as to what "disease" one would endeavor to treat. Similarly, it is alleged that one would seek to obtain such a composition substantially enriched in a specific cell type to study expression of the receptor in the cells. Such a 'motivation', however,

would appear to be a broad conclusory statement that is not supported by a clear or particular showing in any of the references. As such, Applicant maintains that, absent the subject application, one of ordinary skill in the art would not have been motivated to combine the cited references and, therefore, that a *prima facie* case of obviousness has not been established.

Notwithstanding Applicant's position as set forth above, in order to advance prosecution of the subject application, claim 1 has been amended to indicate that a method of the invention allows obtaining a composition substantially enriched in a specific progenitor cell type. Applicant submits that, prior to the present disclosure, it was not known that progenitor cells of a specific lineage could be obtained using a binding agent specific for a serpentine receptor expressed by such cells and indicative of the lineage, and, therefore, one of ordinary skill in the art would not have known to obtain such cells and would have had no reasonable expectation of obtaining such progenitor cells. Furthermore, the cited references, either alone or in combination, do not teach or suggest a method of obtaining a composition enriched in a specific progenitor cell type. Accordingly, it is respectfully requested that the rejection of the claims under 35 U.S.C. § 103(a) be removed.

With respect to claims 2, 3 and 50 to 57, it is submitted that even if for argument sake it is considered that the artisan may have been motivated to combine the cited references, there is nothing in the references, either alone or in combination, that would have led the artisan to further separate, from among those cells selected using a binding agent specific for a serpentine receptor, cells that further express at least one additional marker. As such, it is submitted that the subject matter of claims 50 to 57 (and new claims 61 to 64) would not have been obvious in view of the cited references, either alone or in combination, and, therefore, respectfully requested that the rejection of claims 50 to 57 under 35 U.S.C. 103(a) be removed. With respect to claims 2

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and 3, it is submitted that the issue is moot in view of the amendment to claim 1, from which claims 2 and 3 depend.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect respectfully is requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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Enclosure: Exhibit A

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EXHIBIT A

MARKED-UP COPY SHOWING AMENDMENTS TO THE CLAIMS

Claims 1 and 5 were amended as follows:

1. (Twice amended) A method of obtaining a composition substantially enriched in a specific progenitor cell type comprising:

contacting a sample of cells with at least one binding agent specific for a serpentine cell surface receptor indicative of a specific progenitor cell type or lineage such that the binding agent binds specifically to a progenitor cell or progenitor cells expressing the receptor in the sample; and

separating the cell or cells bound by the binding agent from the sample, thereby obtaining a composition substantially enriched in a specific progenitor cell type.

5. (Twice amended) The method of claim 4, wherein the antibody is a monoclonal antibody, a polyclonal antibody, or [a derivative] an antigen binding fragment of said antibody.